REMARKS

In view of the foregoing claim amendments and following remarks, reevaluation and further processing of the application is requested. A request for continued application is being filed with this amendment. Claim 2 has been amended. Claims 3 to 14 are canceled. Claims 1 and 2 are pending.

The Examiner objects to the specification for the introduction of new matter to the specification in paragraph 3 of the Final Office Action. The Examiner asserts that the previous changes made to pages 12 and 13 (paragraph 64) of the specification constitute new matter.

The Applicant respectfully disagrees with the Examiner. The Examiner previously requested that each peptide in the original specification receive a unique SEQ ID NO. Subsequently, in the previous substitute specification, filed 10/11/05, page 3, original peptide (1_1) was designated SEQ ID NO: 1, original peptide (2) was designated SEQ ID NO: 2, original peptide (3) was designated SEQ ID NO: 3, original peptide (1_2) became SEQ ID NO: 4, original peptide (1_3) was designated SEQ ID NO: 5, original peptide (1_4) was designated SEQ ID NO: 6, original peptide (1_5) was designated SEQ ID NO: 7, original peptide (1_6) was designated SEQ ID NO: 8 and original peptide (1_7) was designated SEQ ID NO: 9. Since the original SEQ ID NO. 1 [original peptides (1_1), (1_2), (1_3), (1_4), (1_5), (1_6), and (1_7)] by subsequent designation became SEQ ID NOS: 1, 4, 5, 6, 7, 8, and 9, at the request of the Examiner, no new matter was added to the specification by the previous substitute specification. Thus, the changes to pages 12 and 13 (paragraph 64) are not new matter. The fact that any or all of the peptides SEQ ID Nos. 1-9 can be used is further supported by, for example, original claims 1 and 3 of the specification and paragraph 14 of the substitute specification filed July 6, 2007.

In paragraph 3 of the Final Office Action, the Examiner objects to an amendment to paragraph 64, lines 8-12 in the specification: "The pharmaceutical compositions of a first embodiment of the invention comprise at least one lyophilised peptide of SEQ. ID: NO. 1 to 39 in dry form, which can be readily dissolved, e.g. in phosphate-buffered saline (PBS), aqua ad injectabilia, Ringer's solution or the like, prior to use."

Support for this amendment is found in paragraph 64 line 3-6: "In the therapeutical methods of the invention a pharmaceutical composition which comprises a therapeutically

effective amount of at least one peptide with an amino acid sequence as disclosed herein in SEQ. ID. NO. 1, 2, 3, 4, 5, 6, 7, 8 or 9 is administered to a patient." Further support can be found, for example, on p. 14 of the original specification where peptide (1_1) is defined as SEQ ID NO: 1, peptide (1_2) is defined as SEQ ID NO: 2, and so on to peptide (1_7) which is defined as SEQ ID NO: 7. However, if the Examiner maintains this objection despite these arguments, the Applicant hereby agrees to amendment of the specification at paragraph 64 to revert to: "The pharmaceutical compositions of a first embodiment of the invention comprise at least one lyophilised peptide of SEQ ID NO: 1 to 3 [[9]] in dry form, ...", by Examiner's amendment.

The Examiner maintains the objection to the Declaration in the Final Office Action. A new Declaration was filed electronically in the USPTO on September 24, 2007. It is hoped that the newly filed Declaration will overcome the Examiner's objection.

The Examiner rejects claims 1 and 2 under 35 U.S.C. 112, first paragraph, in the Final Office Action. Pending claims 1 and 2 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner states as previously set forth that the peptides of the claims are fragments of histone proteins. For example, the Examiner points out that the peptide of SEQ ID NO: 6 appears to be a fragment consisting of amino acids 195-220 of the human histone H1 peptide. The Examiner also states that the peptides are asserted to comprise antigenic determinants of SLE, RA, systemic sclerosis, scleroderma; and the peptides are disclosed as being used for diagnosis and treatment of said diseases.

Regarding treatment of disease, the Examiner alleges that the specification offers just a single paragraph at page 12 wherein it is disclosed that diseases such as SLA, RA and scleroderma can be treated by administration of the claimed peptides. The Examiner states no data is disclosed, and no theory or mechanism by which the peptides might provide an effective treatment is proposed.

Regarding diagnosis of disease, the Examiner alleges the specification discloses only the combination of H1(187-211) and H2B (1-35) peptides bound antibodies from the sera of certain patients. The Examiner cites a lack of sufficient working examples or data relevant to the use of the claimed peptides, thus it would take undue trial and error to practice the claimed invention.

The Applicant respectfully disagrees with the Examiner. The specification provides numerous examples of use of the claimed peptides by methods known to one skilled in the art at the time of invention. For example, paragraph 12 of the instant application discusses a therapeutic method of the invention which exploits monoclonal antibodies and monoclonal antiidiotypical antibodies directed against the autoantibodies of said autoimmune patients. Such monoclonal and antiidiotypic antibodies are claimed in the parent application, now issued U.S. patent to Zeppezauer et al., US 6,369,203. Paragraph 13 discloses a therapeutic method for prevention of the formation of autoantibodies or reduction of their concentration in the body in order to prevent or delay the onset and/or the development of these syndromes in which the formation of autoantibodies plays a role in pathogenesis and/or progression. Methods of production of monoclonal antibodies and monoclonal antiidiotypical antibodies which are reliant upon use of the peptides are disclosed in the instant application. In addition, methods of production of monoclonal antibodies was well-known, and highly predictable, in the art at the time of filing; for example, see Laskov et al., "Monoclonal autoantibodies to histones from autoimmune NZB/NZW F1 mice", Eur. J. Immunol., 1984: 14, 74-81; a copy of which was included with IDS filed July 24, 2007, and which is cited on the face of the parent patent US 6,369,203.

Paragraph 14 discloses peptides with antigenic or immunogenic determinants, recognized by autoantibodies in a patient suffering from an autoimmune disease, where at least one of the peptides or their effective parts (at least an amino acid sequence of at least 8 amino acids) are selected from the group consisting of SEQ ID NOS: 1-9. At the time of filing, methods of peptide synthesis were generally understood by one skilled in the art, so long as the peptide sequence is known (peptide sequences are given in paragraph 14). The fact that a greater proportion of human SLE autoantibodies recognize peptide fragments of histone proteins than the full length histone proteins was known to one skilled in the art at the time of filing. For example, see Muller et al., "Reactivity of autoantibodies in systemic Lupus erythematosus with synthetic core histone peptides", Int. Arch. Allergy Immunol. 1989, 89:288-296; a copy of which was included with IDS filed July 24, 2007.

Paragraph 25 discloses the epitopes of autoantibodies of rheumatic and SLE patients were charted with H1, H2B, and H2A peptides wherein 80% of the SLE sera and 66% of all sera reacted positively to both the C terminus of H1 and the N terminus of H2B. Both structural data

and antigenicity calculations were utilized to determine homologous epitopes of the patient's own antibodies with dominant antigenic character of the N terminus of H2B and the C terminus of H1.

Paragraph 26 discloses an ELISA protocol utilizing either antibodies or antigens to be tested. Paragraph 27 discloses results of one specific ELISA utilizing SLE sera and two peptides corresponding to an N-terminal range (1-35) H2B and C terminal range of (187-211) of H1. Paragraph 29 discloses 68% of sera tested were positive to both peptides.

Paragraphs 30 to 38 describe a method of production of monoclonal anti-histone antibodies directed against the autoantibodies of SLE patients. Paragraphs 31 and 32 disclose the steps of analysis of the histone sequences by mathematical model and prediction of the antigenic ranges. Paragraph 33 discloses a step in the method comprising synthesis of the deduced peptides in accordance with the antigenic ranges, both in free condition and bound to, for example, a TentaGel carrier. Paragraph 34 discloses immunization of mice with synthetic peptides bound to the carrier. Paragraph 35 describes further use of the peptides for the step of immunization of spleen cells and fusion with cancer cells to give hybridoma cells and selection of individual positive clones. Methods of production of monoclonal antibodies were well known, and highly predictable in the art at the time of filing; for example, see Laskov et al., "Monoclonal autoantibodies to histones from autoimmune NZB/NZW F1 mice", Eur. J. Immunol., 1984: 14, 74-81; a copy of which was included with IDS filed July 24, 2007, and which is cited on the face of the parent patent US 6,369,203.

Paragraphs 39 to 57 disclose production of antiidiotypic antibodies; including selection of antigen as an epitope directed against histone peptides H1(187-211) and H2B (1-35); or the corresponding epitope on the monoclonal antibodies which were produced against the peptide or peptide combination.

Paragraph 45 describes use of the peptide epitopes to isolate and enrich SLE autoantibodies by affinity chromatography, wherein the peptides are bound to the affinity column using chemical or absorptive methods. Paragraphs 46 to 47 described other methods of isolation, enrichment, and purification of SLE autoantibodies which employ disclosed peptides.

Paragraphs 50 to 57 discloses use of enriched autoantibodies in the conventional manner for immunization and production of monoclonal antiidiotypic antibodies.

Paragraph 62 discloses use of TentaGels as a synthetic carrier for immunization with disclosed peptides. Specifically, in paragraph 62, "it was possible to use TentaGels as a new synthetic carrier material for successful in vitro immunization. TentaGels constitute a new class of grafted copolymeric particles, whose polystyrene nucleus is surrounded by "marginal bush-like" polyoxyethylene tentacles. These carriers may be employed in a "single step method" after peptide synthesis immediately for in vitro immunization."

Paragraph 63 discloses use of produced antibodies in different immunological test systems well known in the art such as ELISA, immunodiffusion, dot blot and hemaglutination, Western blot and flow cytometry.

Use of antibodies were known to one skilled in the art at the time of filing. For example, specific ELISA techniques employing antibodies are described in the issued parent patent US 6,369,203, col. 2, lines 21-57. Evaluation of immune response by ELISA is also described, for example, in Atanassov et al., "New Zealand white rabbits immunized with RNA-complexed total histones develop an autoimmune-like response" Clin. Exp. Immunol. 1991, 86:124-133, provided in IDS filed in the parent US 6,369,203 and in IDS in instant application filed Sept. 24, 2007.

Discussion of monoclonal antibodies and monoclonal antiidiotypic antibodies use of disclosed peptides for said diseases is disclosed in paragraphs 64 and 65.

Further, the theory of idiotypic mimicry of biological receptors was know in the art at the time of filing; for example, see Gaulton and Greene, "Idiotypic Mimicry of Biological Receptors" Ann. Rev. Immunol. 1986, 4:253-280; a copy of which was included with IDS filed July 24, 2007, and which is cited on the face of the parent patent US 6,369,203.

Thus, the disclosure provides an ample number of uses for the disclosed peptides for both therapeutic and diagnostic purposes, via methods which were well-known to one skilled in the art at the time of filing.

The Examiner rejects claim 2 under 35 U.S.C 112, first paragraph, as failing to comply with the written description requirement in paragraphs 8 and 9 of the Final Office Action. Specifically, the Examiner found no support for the peptide of the claim comprising limitations such as "from 8 to 24 amino acids" or "five contiguous amine acids" has been cited and none has been found.

The Applicant respectfully disagrees with the Examiner. Support for the "from 8 to 24 amino acids" can be found in the specification at paragraph 14, last sentence, which states:

"...that at least one of the following peptides or their effective parts (at least an amino acid sequence of at least 8 amino acids) are selected from the group consisting of

(1_1) KPKAA KPKAA KPKAA KPKKA APKKK, (SEQ ID NO. 1)

(1_2) KPKAA KARVT KPKTA KPKKA APKKK (SEQ ID NO. 4)

(1_3) AAKAV KPKAA KPKVV KPKKA APKKK (SEQ ID NO. 5)

(1_4) KPKAA KPKSG KPKVT KAKKA APKKK (SEQ ID NO. 6)

(1_5) KPKAA KPKTA KPKAA KPKAA AAKKK (SEQ ID NO. 7)

(1_6) KPKAA KPKAA KPKAA KAKKA AAKKK (SEQ ID NO. 8)

(1_7) KPKAA KPKAA KPKAA KP KAKKA AAKKA (SEQ ID NO. 9)

(2) PEPAK SAPAP KKGSK KAVTK AQKKD GKKRK RSEKE, (SEQ ID NO. 2) and

(3) SYSVY VYKVL KQVHP DTGIS SKAMG IMNSF VNDIF ERIAGE (SEQ ID NO. 3)." (emphasis added).

The original "at least eight" encompasses peptides of eight or greater amino acids in length. Further support for the "from 8 to 24 amino acids" is also found in the specification at paragraph 14, last sentence, wherein the shortest peptide sequence is 25 amino acids; however, to claim from 8 to 25 amino acids would cause redundancy with claim 1; hence the claim was amended to 8 to 24 amino acids. Because "at least eight" encompasses "from 8 to 24 amino acids"; we believe this portion of the claim amendment has support in the specification.

Support for the "five contiguous amino acids" portion of the claim amendment can be found in paragraph 24: "...smaller peptides may be selected which contain at least eight amino acids and at least one consensus sequence (depicted as boxes of five amino acids)..." (emphasis added). To one skilled in the art, a box of five amino acids may be understood as five contiguous amino acids. The Applicant thus believes there is support for this amendment.

In light of the above amendments and remarks, it is believed that the application is now in condition for allowance, and such action is respectfully requested. If the Examiner believes that it would be helpful to discuss any of the amendments or remarks presented herein, the Examiner is invited to contact the undersigned at the telephone number provided below.

A supplemental IDS and an RCE Form PTO/SB/30 accompanies this filing. It is not believed that further additional fees are due in connection with this correspondence. However, any necessary additional fees may be charged or overpayments may be credited to Deposit Account No. 50-2775.

Respectfully submitted,

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